

WHAT IS CLAIMED IS:

1. An isolated infectious Respiratory Syncytial Viral (RSV) particle which comprises an RSV antigenome or 5 genome containing at least one lethal deletion in the M2-ORF1 gene.

Sub 23
C2
2. An isolated infectious RSV particle which comprises a chimeric RSV antigenome or genome encoding 10 antigenic polypeptides of both RVS-A and RSV-B.

3. An isolated infectious RSV particle having an attenuated phenotype comprising an RSV antigenome or genome containing an L gene mutation. 15

4. The isolated infectious RSV particle of Claim 1, 2, or 3 which further comprises a heterologous sequence.

5. The isolated infectious RSV particle of Claim 4 20 in which the heterologous sequence is derived from the genome of influenza.

6. A recombinant RNA molecule comprising a binding site specific for a RSV RNA-directed RNA polymerase of a 25 negative strand RNA virus operatively linked to a RSV RNA containing a deletion in M2-ORF1 or M2-ORF2 and further containing a heterologous RNA sequence comprising the reverse complement of a coding sequence.

30 7. The recombinant RNA molecule of Claim 6 in which the heterologous sequence is derived from the genome of a virus other than RSV.

8. The recombinant RNA molecule of Claim 6 in 35 which the heterologous sequence is derived from the genome of another strain of RSV.

9. The recombinant RNA molecule of Claim 8 in which the heterologous coding sequence encodes G or F gene products.

5 10. The recombinant RNA molecule of Claim 6 which further comprises a mutation in the L gene.

11. The recombinant RNA molecule of Claim 6 which further comprises a mutation in the SH gene.

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12. A method of producing a chimeric RSV virus, comprising culturing a host cell containing nucleotide sequences encoding the N, P and L gene products of RSV and the RSV antigenome or genome in the absence of expression of the RSV M2-ORF.

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Sub 4

13. A vaccine comprising a chimeric RSV the genome of which contains the reverse complement of an mRNA coding sequence operatively linked to a polymerase binding site of an RSV and a pharmaceutically acceptable carrier.

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14. The vaccine of Claim 13 in which the mRNA coding sequence encodes a mutated SH gene.

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15. The vaccine of Claim 13 in which the mRNA coding sequence encodes a mutated L gene.

16. The vaccine of Claim 13 in which the mRNA coding sequence encodes a mutated NS1 gene.

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17. The vaccine of Claim 13 in which the mRNA coding sequence encodes a mutated M2 gene.

18. The vaccine of Claim 13 in which the mRNA coding sequence encodes G and F genes of both RSV A and B.

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19. The vaccine of Claim 13 which encodes a heterologous gene.

20. The vaccine of Claim 19 in which the 5 heterologous gene is derived from the genome of influenza.

21. An attenuated genetically engineered RSV containing at least one modified viral gene sequence so at least some defective particles are produced during each round 10 of viral replication in a host.

22. The attenuated virus of Claim 21 in which the sequence modified is a non-coding region that results in down-regulation of synthesis of a viral gene.
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23. The attenuated virus of Claim 21 in which the sequence modified gene sequence encodes at least one insertion, deletion, or substitution of an amino acid residue or epitope.
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24. A pharmaceutical composition comprising the attenuated phenotype of Claim 22 or 23.
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